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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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DICKSTEIN SHAPIRO LLP
1633 Broadway
NEW YORK, NY 10019

EXAMINER

NOAKES, SUZANNE MARIE

ART UNIT	PAPER NUMBER
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1656

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09/08/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/584,718	Applicant(s) TSUCHIDA ET AL.	
	Examiner SUZANNE M. NOAKES	Art Unit 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-5 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/29/2006 & 03/09/2007</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the Claims

1. Claims 1-5 are pending and subject to examination on the merits.

Information Disclosure Statement

2. The information disclosure statements (IDS) submitted on 08/29/2006 and 03/09/2007 have been considered by the examiner. See initialed and signed PTO-1449's. Any reference indicated as not considered (e.g. lined through) has been indicated as such because no English translation of the cited document has been provided.

Claim Objections

3. Claims 2 and 3 objected to because of the following informalities:

(a) Claim 2 recites the method of claim 1, wherein the step of deep-freezing and preserving the RBC's comprises a step of; the claim subsequently lists four additional steps for deep-freezing and preserving. However, it is unclear if the claim intends that all four steps need to be included in the deep-freeze/preserving methodology, or the way the claim currently is written, one skilled in the art need only select one of the four steps such as the deep-freezing the RBC's. It is thus suggested the claim reads as: "...., wherein the step of deep-freezing and preserving the RBC's comprises the steps of;

(b) Claim 3 would be more grammatically complete if written: "The method according to claim 2, wherein the term from the time the red blood cells are.....".

Appropriate corrections are required.

Claim Rejections - 35 USC § 112 – 2nd paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(A) Claim 1 reads on a method of purifying hemoglobin from red blood cells, “wherein the red blood cells are deep-frozen and preserved, and then purified”. However, the claim is confusing because it is unclear whether and then purified part of the claim is qualifying the red blood cells or the hemoglobin. The rest of the dependent claims only talk about the steps for deep-freezing and preserving and say nothing about any steps of purification (of either red blood cells OR hemoglobin). Thus, said dependent claims do not remedy the noted deficiency of independent claim 1.

(B) Claim 2 recites the limitation “preserving the extracted red blood cells at 4°C - 10 °C....” in reference to claim 1. There is insufficient antecedent basis for this limitation in the claim because there is no active step or no step at all in either claims 1 or 2 which recites an extraction process.

(C) Claims 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: the extraction of the hemoglobin

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from the red-blood cells by thawing the stored RBC's, lysing said RBC's and then purifying the hemoglobin from the lysed RBC's.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 1-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tye (US 4,473,494 – cited on IDS) in view of Castino et al. (J. of Mem. Sci, 1996, 110:169-180) and Abersold et al. (US 5,856,082).

The claims are drawn to a method of purifying hemoglobin (any form) from red blood cells (RBCs) by deep-freezing and preserving said RBCs (claim 1), wherein said RBC's can be extracted and kept at 4-10°C, washed, deep-frozen (at a temperature lower than -60°C) and/or preserved in said deep-frozen state (claim 2), at a temperature lower than -60°C and wherein the time frame of extracting said RBC's until they are deep-frozen is 1-60 days (claim 4).

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Tye teaches a method of purifying "stromal-free" tetrameric hemoglobin by starting with red blood cells of freshly drawn, outdated, or frozen packed cells or whole blood. The blood is drawn in sterile fashion into containers with sufficient anticoagulant activity to prevent clot formation. Hemoglobin from a variety of mammalian sources, such as human, bovine, ovine, or porcine are disclosed to be useful. Any non-heme protein is removed, preferably by zinc precipitation. Hemoglobin is released from the red blood cells by hypotonic lysis or can be released by the well-known "freeze-thaw" method (see column 4, lines 47-56), followed by ultrafiltration and purification of the hemoglobin.

Thus, Tye teaches a method of purifying hemoglobin from already frozen RBC's, and/or wherein the lysis/extraction of hemoglobin for purification is performed by freezing the RBC's and thawing said RBC's in order to lyse said cells. Tye, however, does not teach the temperature at which the freezing takes place, e.g. a deep-freeze temperature of -60°C or below.

Castino et al. teach that as of 1996 (e.g. date of publication), the cryopreservation of human blood products was routine. They also teach that freezing and thawing of RBC's (haemolysis) leads to an increased concentration of hemoglobin in the supernatant (see p. 169, 2nd column, 1st full paragraph) which is inherently due to hemoglobin being released by the lysed cells.

Absersold et al. provide an example of the common freeze-thaw lysis method of cells by freezing various cells in liquid nitrogen, e.g. deep-freezing the cells (see the

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instant specification's own Example 5) and thawing the cells for three-cycles in order to completely lyse said cells.

Therefore it would have been obvious to one of ordinary skill in the art at the time the invention was made to purify hemoglobin according to the method of Tye et al. from red blood cells by performing the well known "Freeze-thaw" mode of lysing RBC's, wherein said freezing takes place at cyro-temperatures, e.g. deep-freeze temperatures which is generally regarded as -80° or below (which liquid nitrogen is well known to be at a temperature of -196°C), because Castino et al. note that this increases the concentration of hemoglobin in the supernatant and that cryopreservation of blood products has been well established. Furthermore, Tye teaches that RBC's can be lysed by this method and Abersold et al. provide a precise methodology and example of this method by freezing cells in liquid nitrogen (-196°C) followed by thawing said cells.

One skilled in the art would have a high expectation of success in doing so because the hemoglobin purification strategy as set-forth by Tye is already proven, however, it only lacks the information regarding the requisite degree of freezing for lysing the RBC's for hemoglobin purification. This information, however, is readily available as exemplified and taught by Abersold et al.

Hence the claimed invention is considered *prima facie* obvious in view of the prior art.

References of Interest – Not Relied Upon

8. Posner et al. (US PG-Publication 2005/0175977) teach a method of producing glycosylated hemoglobin wherein the method comprises steps including separating human red blood cells from anti-coagulated blood, washing the human red blood cells with physiological saline and centrifuging the red blood cells and aspirating and discarding a resulting supernatant and a white blood cell layer, lysing the packed red blood cells, mixing and freezing the cell/water mixture, defrosting, centrifuging, filtering and saving the supernatant, heating the supernatant, diafiltering the adjusting the hemolysate so that a final hemoglobin concentration is within specified limits. (see Abstract, paragraphs 0030-0042 and claims 1-9). It is noted that there is nothing in the claims that requires that RBC are intact or whole when placed in a deep-frozen state rather than in a lysed state and all claims are open (e.g. comprising which can encompass additional steps).
9. Valeri (Transfusion, 1975, 15(3):195-218) teach methods of cryo-preserving RBC's.

Conclusion

10. No claim is allowed.
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUZANNE M. NOAKES whose telephone number is (571)272-2924. The examiner can normally be reached on 7.00 AM-3.30 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SUZANNE M. NOAKES/
Primary Examiner, Art Unit 1656
03 September 2009